

follow-up, the occurrence rate of the major cardiac adverse event was similar between the patients with extensive metabolizers and with poor and intermediate metabolizers (19 (9.5%) vs. 21 (8.4%),  $p=0.73$ ). Survival analysis revealed similar MACE rates in patients with poor and intermediate metabolizers with respect to extensive metabolizers.

**CONCLUSION** Among Korean patients treated with clopidogrel for PCI, carriage of even one reduced function CYP2C19 allele appears to be associated significantly with an increased level of PRU and a higher incidence of High on-treatment clopidogrel platelet reactivity but both the platelet reactivity and gene polymorphisms did not predict major adverse cardiovascular events.

#### TCTAP A-024

##### The Importance of Serial Measurement of Platelet Aggregation in Long Term of Dual Antiplatelet Therapy in Drug Eluting Stent Era

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**BACKGROUND** The dual antiplatelet therapy (DAPT) including aspirin and clopidogrel is the standard therapy in percutaneous coronary intervention (PCI). However, the divergent duration of DAPT and the varying response of clopidogrel were two substantial concerns in the era of PCI, especially with drug-eluting stents (DES) implantation. Therefore, we combined them together to evaluate their effect on long term influence on patients undergoing DES.

**METHODS** Patients with coronary artery disease treated exclusively with Cypher sirolimus-eluting stents (SES) or Endeavor zotarolimus-eluting stents (ZES) between September 2006 and June 2009 were screened. Among them patients were eligible for participation in this retrospective analysis if they had undergone PCI implantation since enrollment and not had a major adverse cardiovascular event (death, myocardial infarction, stroke, stent thrombosis or repeat revascularization) within the first year since implantation. All patients were routinely measured AA and ADP during the PCI procedure. And then all of the procedures were performed using standard interventional techniques. The interventional strategy and device utilization, including DES type (SES or ZES), were left to the discretion of the operators. The primary endpoint (MACCE) was a composite of all-cause death, nonfatal myocardial infarction (MI), stent thrombosis, unexpected repeat revascularization, and stroke.

**RESULTS** 1245 suitable patients were analyzed for our purpose. There were 204, 419, 289, 333 patients in the A group (12 month DAPT & low platelet aggregation), B group (>12 month DAPT & high platelet aggregation), C group (12 month DAPT & high platelet aggregation), D group (>12 month DAPT & low platelet aggregation), respectively. Compared with the rest of patients, the D group was associated with decreased incidence of MACCE [HR 0.485, 95%CI (0.25-0.96);  $P=0.038$ ]; when cox proportional hazard models were further tested with the D group as the reference category within the same group, the B and C group were associated with more incidence of MACCE [HR 2.26, 95%CI (1.10-4.68);  $P=0.0273$ ] and [HR 2.31, 95%CI (1.03-5.18);  $P=0.0413$ ]. Their respective multivariate Cox proportional hazards regressions confirmed the tendencies mentioned above. As concerned to MACE, The univariate Cox proportional hazards regression demonstrated the B group, overlapping stents, small vessels, and PVD were also linked to more incidence of MACE. After adjustment by multivariate Cox proportional hazards regression, PVD was still an independent risk factor of the MACCE.

**CONCLUSION** This is the first study that took into account the duration of DAPT and serial measurement of individual platelet function together in the routine clinical practice in the long term. The present study demonstrated the lower mean ADP level could guarantee a clinical benefit in the long term not only in primary endpoint but also in secondary endpoint. This relationship suggested the mean of ADP could better reflect the response of clopidogrel and underlined the importance of serial measurements of ADP in chronic administration. Our study demonstrated serial measurement of ADP level was of importance in long term use of DAPT; The present results demonstrated patients with extension of DAPT above a year with lower ADP level could benefit compared with the rest patients. Further comparisons were made among the four groups, which suggested the B and C groups were risk factors compared with the D group. In other words, it supported the D group was superior to the B and C groups.

#### TCTAP A-025

##### Impact for Discontinuation of Dual Antiplatelet Therapy for Unexpected Reason Within 3 Months After 2nd Drug Eluting Stent Implantation

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**BACKGROUND** To assess the safety of discontinuation of dual antiplatelet therapy (DAPT) for unexpected reason within 3 months after 2<sup>nd</sup> drug-eluting-stent (2<sup>nd</sup> DES) implantation.

**METHODS** A total of 1661 consecutive patients (age  $70\pm 10$  years, male 74%)(2764 lesions) who underwent 2<sup>nd</sup> DES implantation was enrolled. 150 patients (190 lesions) received DAPT within 3 months (short group) and 1577 patients (2526 lesions) received DAPT above 3 months (long group). 34 patients (48 lesions) who stopped both of antiplatelet therapy excluded. The typical reasons to stop DAPT within 3 months were allergy, bleeding and no adherence. Primary outcome was definite and probable stent thrombosis defined by Academic Research Consortium (ARC).

**RESULTS** Patient and lesion characteristics were similar between two groups except age which was higher in short group than long group ( $72\pm 10$  vs.  $69\pm 10$ ,  $p < 0.001$ ). Mean DAPT duration was  $36\pm 33$  days in short group and  $698\pm 386$  days in long group. Aspirin was mainly selected as whole life single antiplatelet therapy in both groups (short 82.4% vs. long 81.7%,  $p=0.82$ ). In follow up term ( $24.7\pm 13.4$  months), the incidence of ST was similar between two groups (1.0% in short group vs. 0.5% in long group,  $p=0.34$ ).

**CONCLUSION** Discontinuation of DAPT for unexpected reason within 3 months after 2<sup>nd</sup> DES implantation did not increase the risk for ST.

#### TCTAP A-136

##### Identifying the Particular Human Plasma Metabolites Which Produces the Best Response from Warfarin Based on International Normalized Ratio

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**BACKGROUND** Warfarin, an anticoagulant drug has been used regularly despite of its bleeding tendency. This adverse effect is usually controlled by checking International Normalized Ratio (INR). The aim of this study is to determine the ability of plasma metabolites to distinguish individuals with different INR stability.

**METHODS** This study focuses on two types of patients; stable INR (2-3) and unstable INR (<2 or >3), 44 patients of stable group, and 50 patients of unstable group, on at least 9-month warfarin treatment. Both groups were selected based on Morisky scale > 6 (medium to high adherence). The INR was monitored for each individual during the last six months of the treatment period. INR case without changes was considered stable. Otherwise, it would be considered unstable. The blood samples were centrifuged and the obtained plasma samples were mixed with phosphate buffer (1:1). The mixture was centrifuged and the supernatant was taken to perform <sup>1</sup>H-NMR experiment. The NMR spectra were binned and the data were analyzed using principle component analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA).

**RESULTS** Fifteen female and 29 male patients (mean age 66.5), treated with the average warfarin dose of 3.08 mg, showed a stable INR while the unstable group including 28 males and 22 females (mean age 64.7) was treated with the average dose of 3.66 mg. No significant difference was observed between two groups with respect to warfarin dose ( $p=0.066$ ), the patient age ( $p=0.415$ ) and gender ( $p=0.332$ ). Three outliers were identified in PCA score plot. The OPLS-DA four-component model (96% accuracy, 97.73% sensitivity, and 96.81% specificity) with  $R^2$  (cum) = 0.575 and  $Q^2$  (cum) = 0.355 revealed a clear separation between the two groups. Through the VIP plot, the discriminatory metabolites were determined.

**CONCLUSION** The plasma metabolomics technique able to differentiate the plasma metabolic profiles of the patients on warfarin with stable and unstable INR. Validations of the metabolites with more subjects are ongoing.